# Case

- 36 year old male
- No significant PMH
- CC: recurrent clear rhinorrhea alternating with congestion

# Case

- Seasonality
  - Perennial with worsening in the winter months
- Denies any sneezing or pruritus
- No ocular or skin symptoms
- No wheezing or other pulmonary symptoms

# Case

- Exposures
  - Pets: one cat, no dogs
  - No specific environmental controls at home
  - No tobacco exposure
- Family history
  - Brother with “severe allergies”
- Physical exam unremarkable

# ALLERGY TEST RECORD - INHALANTS, POLLENS, INSECTS

*(This form is subject to the Privacy Act of 1974 - Use Blanket PAS-DD form 2005)*

## CRITERIA FOR PRICK

1 + Erythema smaller than a nickel in diameter (21mm)
2 + Wheal < 3mm with surrounding erythema
3 + Wheal > 3mm with surrounding erythema
4 + Wheal with pseudopods and surrounding erythema

*Comments:*
**Local Allergens for Region 5*

| | Prick 1:20 | | ID 1:1000 |
|---|---|---|---|
| 1 Control diluent | w / f | 0 | w / f |
| ***Trees*** | | | |
| 2 Ash, White | w / f | 0 | w / f |
| 3 Birch Mix | w / f | 1+ | w / f |
| 4 Box Elder/Maple Mix | w / f | 0 | w / f |
| 5 Cottonwood, Common | w / f | 0 | w / f |
| 6 Elm, American | w / f | 0 | w / f |
| 7 Hackberry* | w / f | 1+ | w / f |
| 8 Mesquite* | w / f | 4+ | w / f |
| 9 Mountain Cedar | w / f | 0 | w / f |
| 10 Mulberry Mix | w / f | 0 | w / f |
| 11 Oak Mix | w / f | 0 | w / f |
| 12 Olive | w / f | 0 | w / f |
| 13 Pecan | w / f | 0 | w / f |
| 14 Sycamore, American | w / f | 0 | w / f |
| ***Grasses*** | | | |
| 15 Bahia | w / f | 0 | w / f |
| 16 Bermuda | w / f | 0 | w / f |
| 17 Johnson | w / f | 0 | w / f |
| 18 Rye | w / f | 0 | w / f |
| 19 Timothy | w / f | 0 | w / f |
| ***Weeds*** | | | |
| ***Chenopod Family*** 20 Burning Bush (Kochia) | w / f | 0 | w / f |
| 21 Lambs Quarters | w / f | 0 | w / f |
| 22 Russian Thistle | w / f | 0 | w / f |
| ***Amaranth Family*** 23 Pigweed/Carless Mix | w / f | 0 | w / f |
| ***Composite Family*** 24 Marshelder/Poverty Mix | w / f | 0 | w / f |
| 25 Ragweed GSW | w / f | 0 | w / f |
| 26 Sagebrush/Mugwort | w / f | 0 | w / f |
| ***Dock/Knotweed Family*** 27 Dock/Sorrell Mix | w / f | 0 | w / f |
| ***Plantain Family*** 28 Plantain, English | w / f | 0 | w / f |

| | Prick 1:20 | | ID 1:1000 |
|---|---|---|---|
| ***Molds*** | | | |
| 29 Alternaria tenuis | w / f | 0 | w / f |
| 30 Aspergillus fumigatus | w / f | 0 | w / f |
| 31 Aspergillus niger* | w / f | 0 | w / f |
| ~~32 Bipolaris*~~ | w / f | N/A | w / f |
| 33 Epicoccum nigrum | w / f | 0 | w / f |
| 34 Fusarium vasinfectum* | w / f | 0 | w / f |
| 35 Helminthosporium interseminatum | w / f | 0 | w / f |
| 36 Hormodendrum cladosporioides | w / f | 0 | w / f |
| 37 Penicillium notatum | w / f | 0 | w / f |
| 38 Rhizopus nigricans* | w / f | 0 | w / f |
| ***Environmentals*** | | | |
| 39 D. pteronyssinus | w / f | 0 | w / f |
| 40 D. farinae | w / f | 0 | w / f |
| 41 Cat Pelt (AP) | w / f | 0 | w / f |
| 42 Dog (AP) | w / f | 0 | w / f |
| 43 Cockroach Mix | w / f | 0 | w / f |
| 44 Feather Mix* | w / f | 0 | w / f |
| ***Other*** | | | |
| 45 Histamine | w / f | 10X20 | w / f |
| 46 | w / f | | w / f |
| 47 | w / f | | w / f |
| 48 | w / f | | w / f |
| 49 | w / f | | w / f |
| 50 | w / f | | w / f |
| 51 | w / f | | w / f |
| 52 | w / f | | w / f |

Name of Patient SSN

Doc



Sta

# Case

- Skin Testing
  - Positive to mesquite only with good positive and negative controls
- Therapeutic trials
  - Improvement with Flonase
  - On separate occasion also noted improvement with Atrovent nasal spray

# Case

- What is the diagnosis?
- What other questions do you want to ask?
- Do you offer immunotherapy for mesquite?

# What To Do When the Skin Tests are Negative

Melinda M. Rathkopf, MAJ, USAF, MC

OIC, Allergy Clinic/Regional Consultant

April 2005

# INTRODUCTION

- Rhinitis may be caused by allergic, nonallergic, infectious, hormonal, occupational, and other factors
- Significant cause of widespread morbidity
- Can impact quality of life – fatigue, headache, cognitive impairment, other systemic symptoms

# INTRODUCTION

- Associated with asthma, sinusitis, and chronic otitis media
- Allergic rhinitis affects 20 to 40 million people in the U.S. annually
  - 10-30% of adults
  - Up to 40% of children
- Estimated cost of AR in 1995 was 2.7 billion dollars

# Rhinitis

- Inflammation of the membranes lining the nose
- Characterized by:
  - Nasal congestion
  - Rhinorrhea
  - Sneezing
  - Itching of the nose
  - +/- Postnasal drainage
- Frequently accompanied by symptoms involving the eyes, ears and throat

# Rhinitis

- Allergic Rhinitis
  - Seasonal and perennial
  - Congestion, rhinorrhea, sneezing, pruritus
  - Common cause of chronic cough
- 50% non-allergic (NAR)
  - Less likely to have sneezing and itching
  - More common in adults than children
  - More likely to have perennial symptoms

# Broad Differential of NAR

- Infectious
  - Viral URI, sinusitis
- Inflammatory
  - NARES, polyps, atrophic rhinitis, granulomatous
- Anatomic
  - Septal deviation, foreign bodies, tumors
- Non-Inflammatory
  - Vasomotor, medications, occupational
- Other
  - Immunodeficiencies, ciliary dyskinesia

# Adult Differential

- Vasomotor (61%)
- NARES (33%)
- Sinusitis (16%)
- BENARS (4%)
- Hypothyroid (2%)

- Nasal polyps
- Deviated septum
- Turbinate hypertrophy
- Medications
- Occupational
- Atrophic rhinitis
- Granulomatous
- Tumors

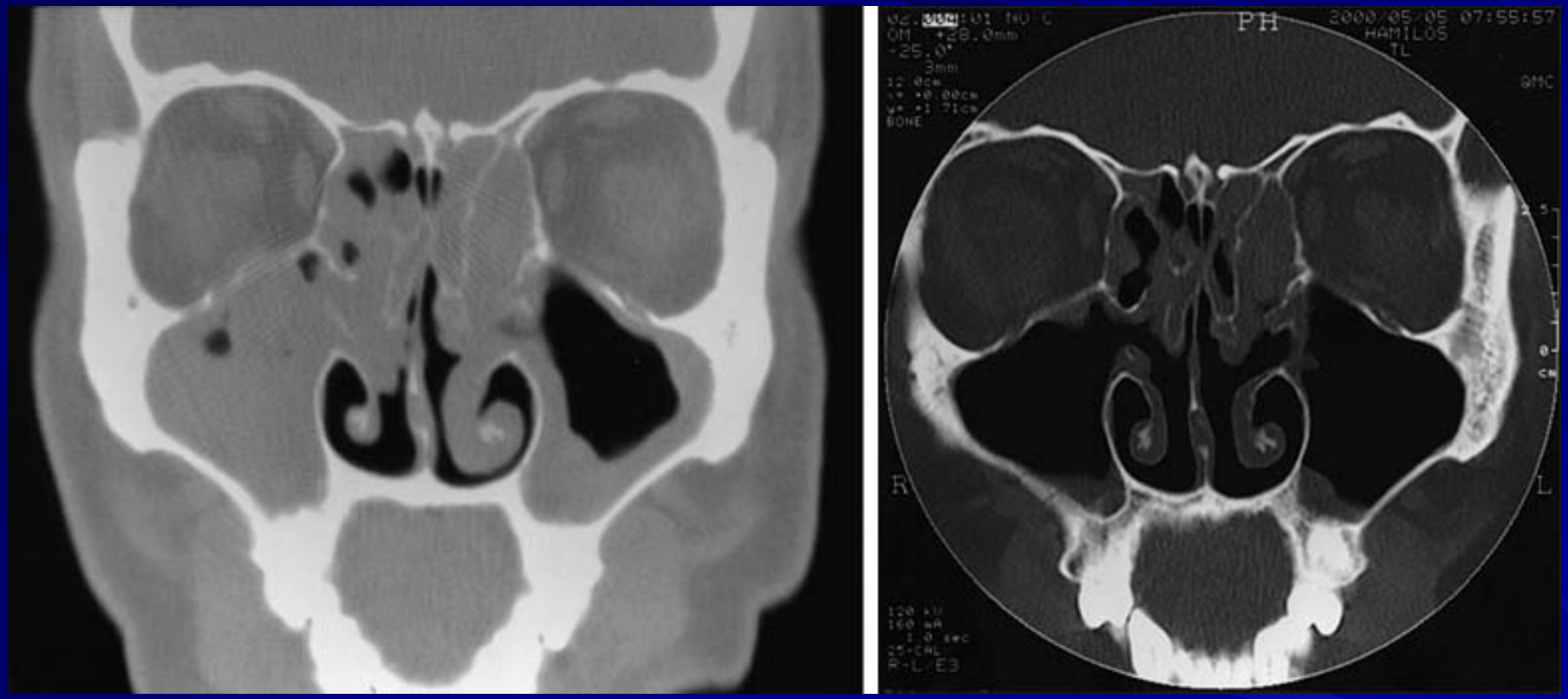
# Pediatric Differential

- Viral URI
- Chronic sinusitis
- Adenoidal hypertrophy
- Septal deviation
- Turbinate hypertrophy
- Foreign bodies
- Choanal atresia
- Nasal polyps
- Immunodeficiencies
- CSF leak
- Tumors

# Infections

- Viral URIs
- Sinusitis
  - Acute
    - 3-8 weeks
  - Chronic sinusitis
    - >8 weeks

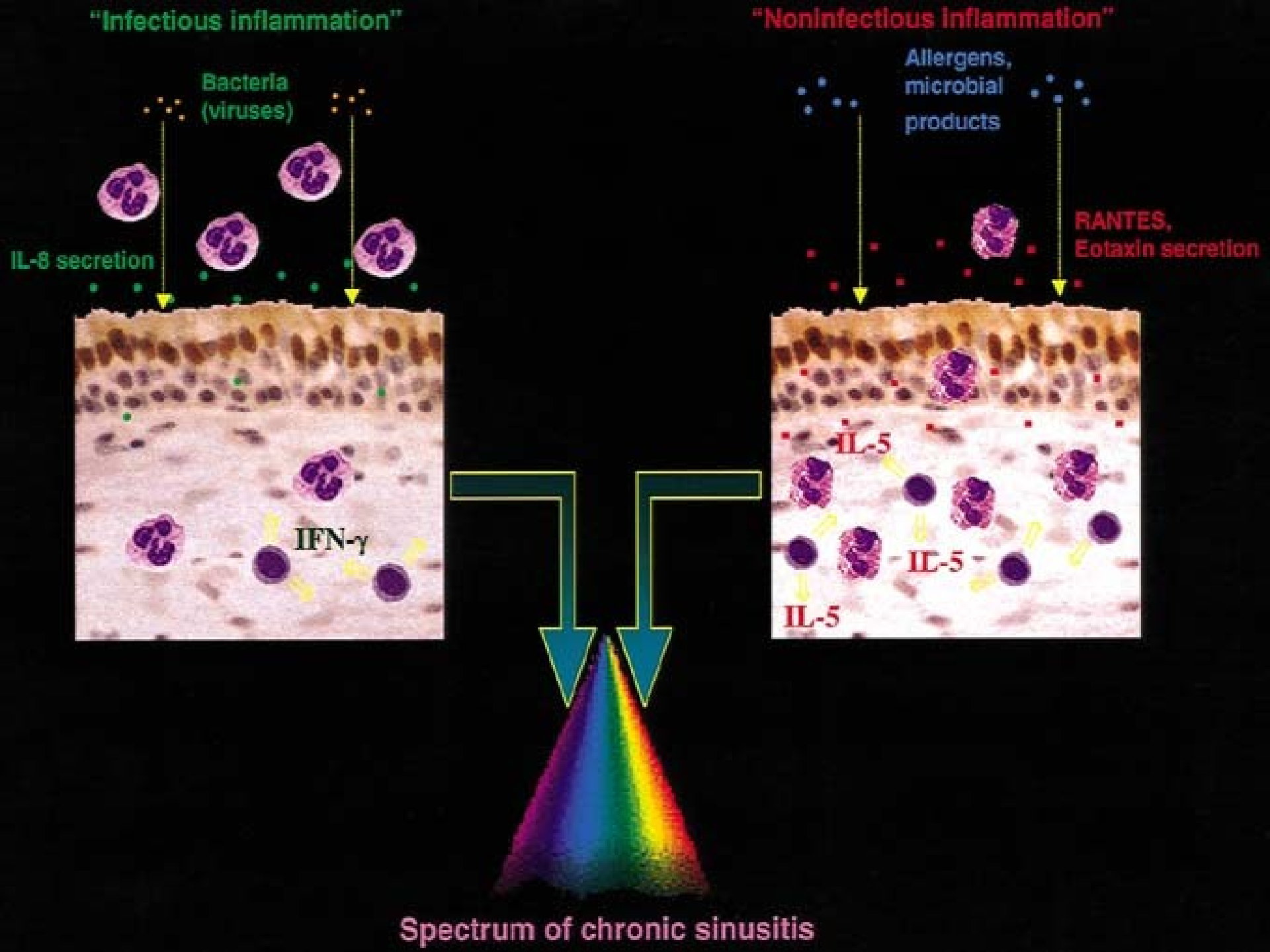
# Chronic Sinusitis




- Affects 13.5% of population
- CT shows mucosal thickening

# Chronic Sinusitis

- Mucopurulent discharge, anosmia, facial pain
- Predisposing conditions
  - Anatomic obstruction, nasal polyps
  - Allergic fungal sinusitis (AFS)
  - Cystic fibrosis, ciliary dysfunction, immunodeficiency
- Often fail antibiotics
  - CT sinuses after 4 weeks of medical treatment


"Infectious inflammation"
Bacteria
(viruses)
IL-8 secretion
IFN-γ
"Noninfectious inflammation"
Allergens,
microbial
products
RANTES,
Eotaxin secretion
IL-5
IL-5
IL-5
Spectrum of chronic sinusitis

# Allergic Fungal Sinusitis

- Recalcitrant sinusitis
- Non-invasive fungal infiltration
- Allergic mucin
- Immunocompetent host
- Skin test sensitivity to molds
  - Bipolaris, Aspergillus

# Inflammatory

- NARES/BENARS
- Nasal polyps
- Atrophic Rhinitis
- Granulomatous

# NARES

- Non-Allergic Rhinitis with Eosinophils
  - 15-30% of adult NAR, middle aged
  - Profuse sneezing, watery rhinorrhea, anosmia
  - Skin test negative
  - Nasal smear shows marked eosinophilia
  - Assoc w/ intrinsic asthma, ASA sensitivity, polyps

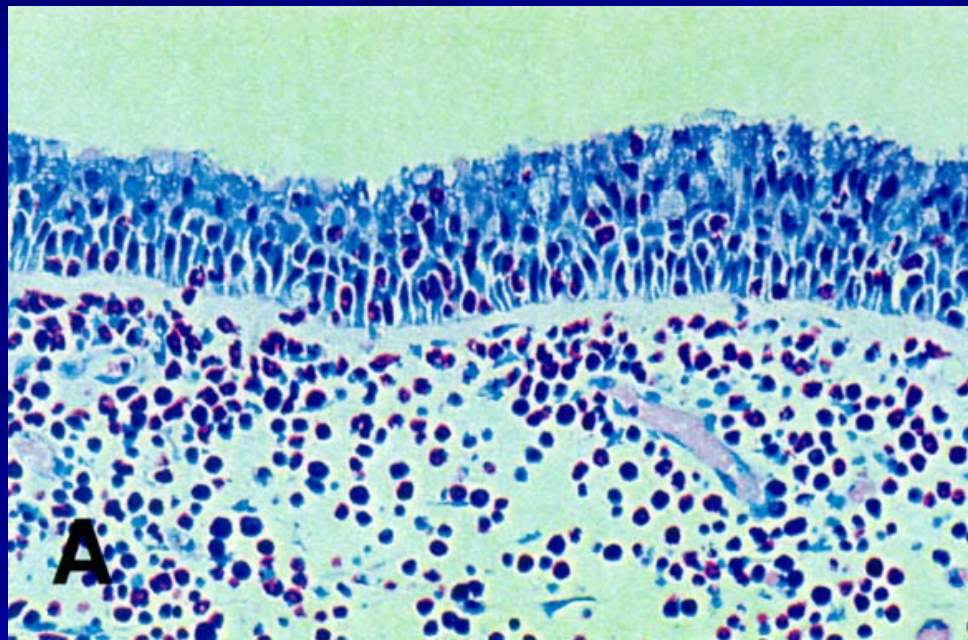
# BENARES

- Blood Eosinophilia Nonallergic Rhinitis Syndrome
  - 4% of adult NAR
  - Subset NARES w/ peripheral blood EOSs

# Nasal Polyps

- Affect 1% population, increase w/ age
  - 40% of adults > 50y/o w/ rhinitis
  - If <16 y/o  evaluate for cystic fibrosis
- Associations
  - ASA sensitivity, asthma, chronic sinusitis
  - CF, ciliary dyskinesia, AFS, Churg-Strauss
  - Not assoc w/ allergies
- Painless, gray, nasal obstruction

# Nasal Polyps



# Atrophic Rhinitis

- Chronic nasal disease
- Progressive atrophy of nasal mucosa
- Resorption of underlying bone (turbinates)

# Atrophic Rhinitis

- Presence of viscid secretion
  - Rapidly dries and forms crusts
  - Emits characteristic foul odor – ozena
    - Leads to social rejection
    - Sleep disturbance
    - Psychotic behavior

# Atrophic Rhinitis

- Primary atrophic rhinitis
  - Cause remains elusive
    - Infectious, hormonal, dietary, vascular, hygienic, developmental and hereditary causes have been postulated
  - Associated with *Klebsiella ozaenae*
  - Chronic, progressive inflammatory process
    - Atrophy and fibrosis
    - Loss of cilia & goblet cells; arteritis obliterans
  - Rare in developed countries

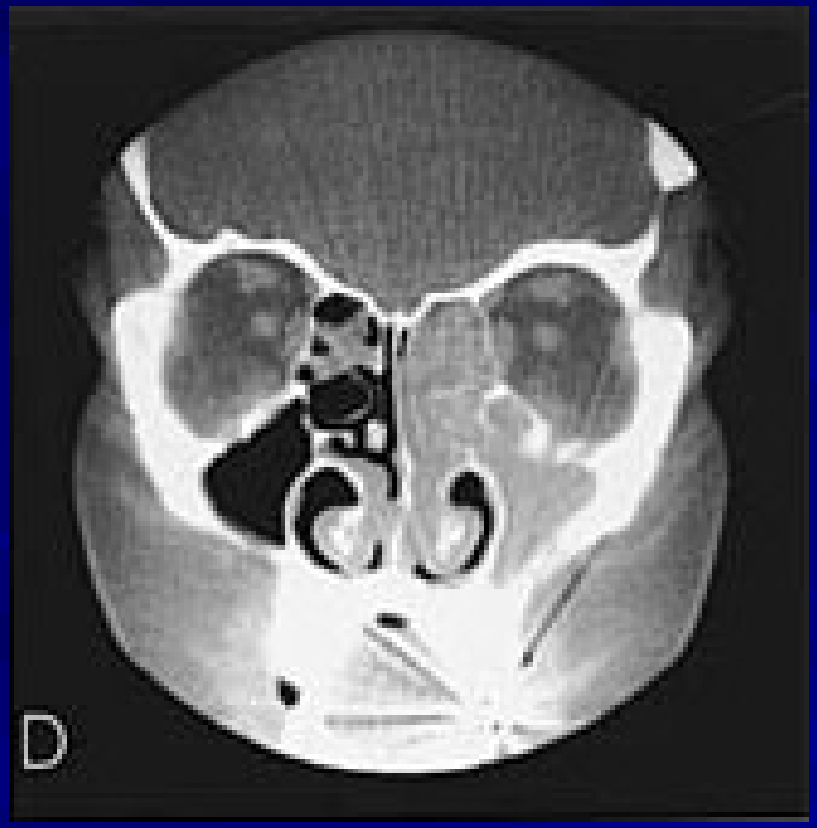
# Atrophic Rhinitis

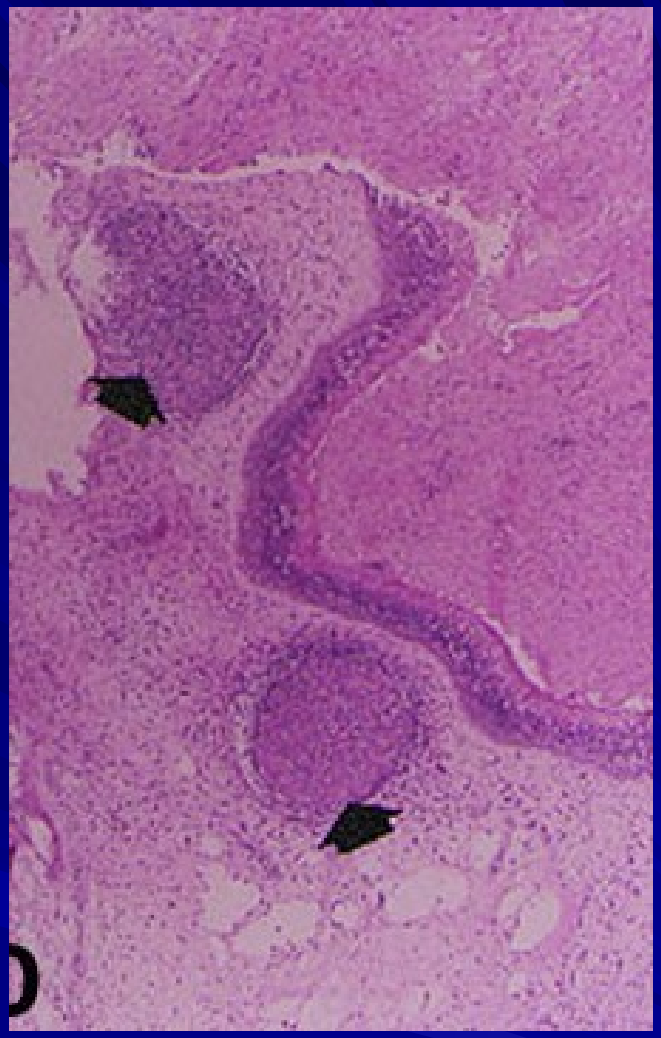
- Secondary atrophic rhinitis
  - Late complication from surgery, radiation, trauma
  - Can be associated with TB or syphilis

# Granulomatous Sinusitis

- TB, syphilis, Wegener’s
- Sarcoid by exclusion
- Can occur w/o pulmonary involvement
- Erythematous, friable mucosa
- Non-caseating granuloma

# Sarcoidosis



# Anatomic

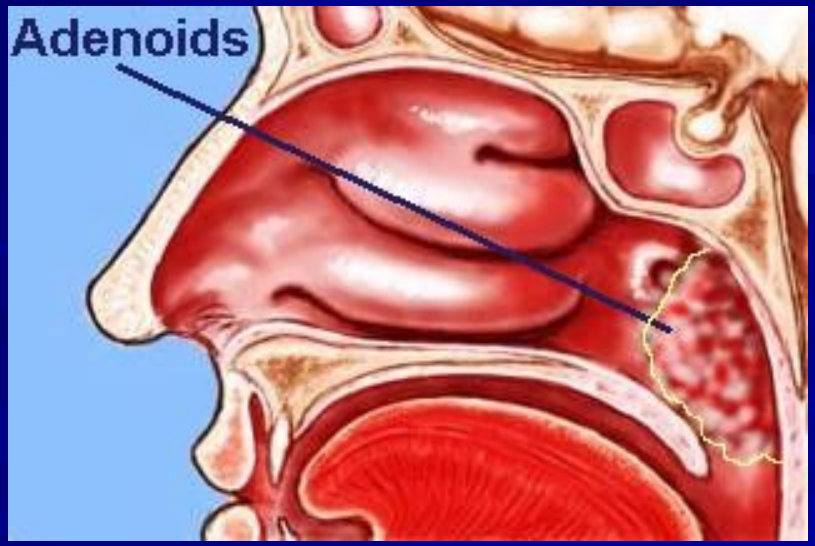
- Septal deviation
- Turbinate hypertroph
- Foreign bodies
- Adenoidal hypertrophy
- CSF Leak
- Tumors

# Anatomic

- Deviated septum / turbinate hypertrophy
  - Mild, well tolerated
  - Only symptomatic when severe
  - Concomitant rhinitis produces congestion
- Foreign body rhinitis
  - Foul-smelling or bloody nasal discharge
  - Small children?

# Adenoidal Hypertrophy

- Most common anatomic cause of nasal obstruction in small children
- Mouth breathing
- Sleep disturbance, snoring



# CSF Leak

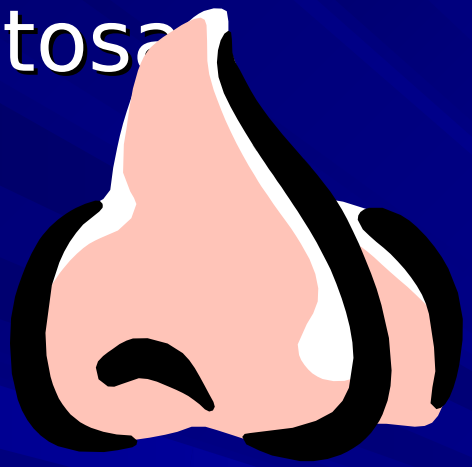
- Refractory clear rhinorrhea
- Occurs in 5% of all basilar skull fractures
- 95% present within 3 months of trauma or surgery
- Fluid has glucose >30mg/dL and presence of $\beta_2$-transferrin
- 50% recover spontaneously
- Consider prophylactic antibiotics

# Neoplasm

- Rare
- Unilateral nasal obstruc
- Unilateral facial pain
- Nasal bleeding

# Non-Inflammatory

- Vasomotor
- Rhinitis medicamentosa
- Occupational
- Hormonal
- Emotional
- Reflex



# Vasomotor Rhinitis

- Common in adults
- Prevalence of 5-10%
- Higher prevalence in females
- Environmental triggers
  - Gustatory rhinitis
    - Hot or spicy foods, alcohol
  - Cold air
  - Irritant
    - Strong smells, temperature variation

# Vasomotor Rhinitis

- May have congestion or rhinorrhea
- Bland nasal smear – no eosinophilia
- Mechanism
  - ? Neurovascular imbalance
  - Term implies increased neural efferent traffic to blood vessels supplying the nasal mucosa – not proven

# Rhinitis Medicamentosa

- Caused by topical or systemic drugs
- Rebound congestion when used >3-5 days
- Erythema, edema, punctate bleeding of mucosa
- Rarely leads to septal perforation

# Rhinitis Medicamentosa

- Causative agents
  - Topical vasoconstrictors
    - Phenylephrine and oxymetazoline
  - Antihypertensives
    - Reserpine, hydralazine, guanethidine, methyldopa, prazosin β-blockers, ACE inhibitors
  - Psychotropic drugs
    - Thioridazine and chlordiazeposide-amitryptiline
  - Ovarian hormonal agents
    - OCPs, cocaine

# Occupational Rhinitis

- 4% of occupational respiratory disease
- Nasal mucosa absorbs soluble aerosols
- Traps particles > 5 μm diameter
- Irritant rhinitis clears when exposure stops
- Cause burning and congestion
- Allergens cause persistent itching, sneezing, rhinorrhea

# Occupational Rhinitis

| Irritant | Allergen |
|---|---|
| Acid/Alkali | Acid anhydrides |
| Ammonia | Latex |
| Bleach | Flour dust |
| Ozone | Animal proteins |
| $SO_2$ | Molds |
| Volatile Organic Cmpd | Grain dusts |
| Pesticides | Isocyanates |
| Chromates | Western Red Cedar |

# Non-Inflammatory Rhinitis

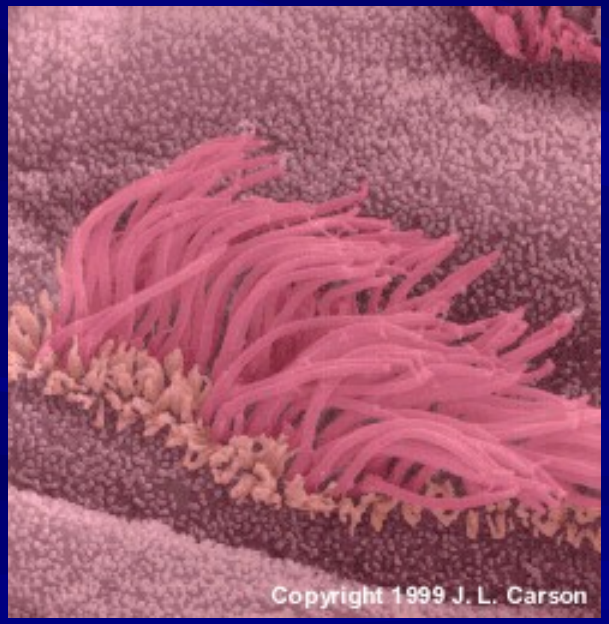
- Hormonal
  - Hypothyroidism
  - Acromegaly
  - High estrogen state/pregnancy
    - ~ 1/3 of pregnant women
    - Hormone-induced nasal vasodilation and enhancement of mucus secretion

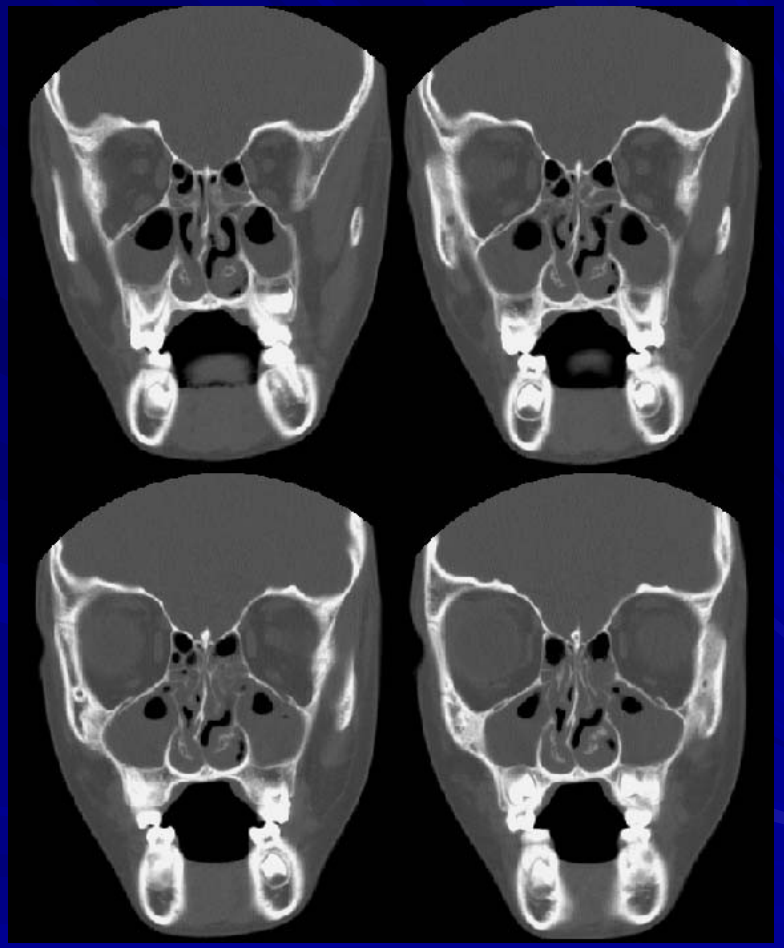
# Non-Inflammatory Rhinitis

- Emotional factors
  - Autonomic stimulation with stress or sexual arousal
- Reflex induced
  - Bright light

# Sinopulmonary disease...

- Immunodeficiencies
- Ciliary dyskinesia

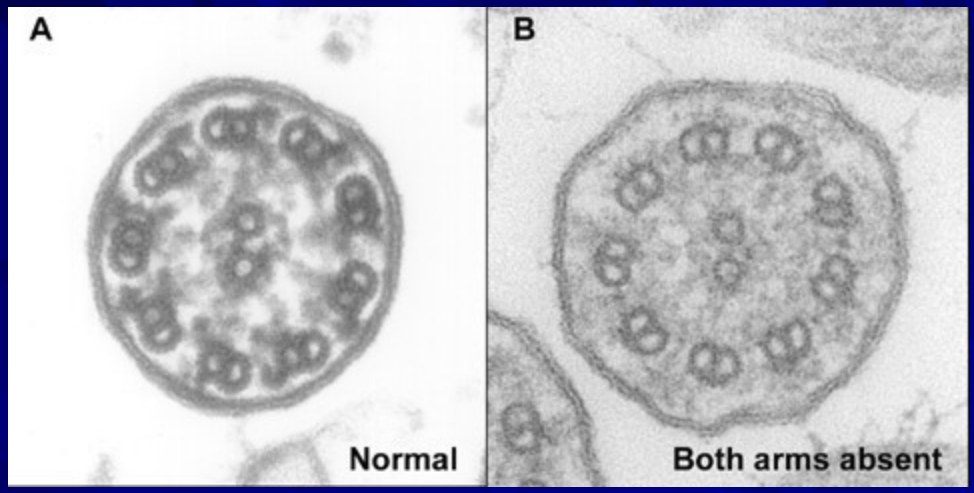


# Immunodeficiencies

- Humoral immunodeficiencies may result in severe sinopulmonary disease
- Usually not subtle
- Selective IgA or polysaccharide antibody deficiency milder
- Recurrent sinusitis

# Ciliary Diskinesia




- Kartagener's
  - Situs inversus, sinusitis, bronchiectasis
  - Infertile males
- Immotile cilia syndrome
  - Early onset chronic rhinorrhea
  - Chronic/recurrent sinusitis
  - Chronic productive cough

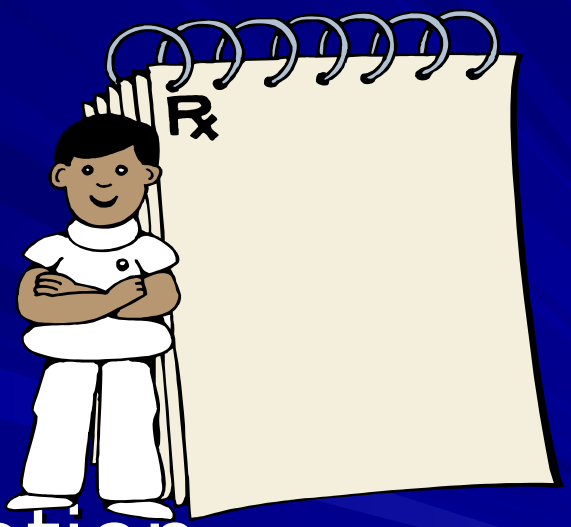
# Treatment

- Underlying cause dictates treatment choices
- Differentiation between inflammatory and noninflammatory useful in selecting therapy
- Anatomic abnormalities and tumors may require surgical intervention
- Remove offending medications in rhinitis medicamentosa
- Treat underlying conditions in secondary rhinitis

# Treatment

- Antihistamines and mast cell stabilizers generally not effective

- Nasal corticosteroids
- Decongestants
- Anticholinergics
- Hypertonic nasal irrigation



# Nasal Corticosteroids

- Anti-inflammatory
  - Shrink nasal polyps and mucosa
- Side effects:
  - Dry nasal mucosa, epistaxis, septal perforation (rare)
  - No effect on adrenocortical function
  - Case reports of ↑ intraocular pressure

# Decongestants

- Oral
  - Pseudoephedrine
  - Combined with Allegra, Claritin and Zyrtec
  - May cause tachycardia and HTN
  - Phenylpropanolamine removed from market (⇑ CVA risk)
  - Long-acting, SR, preparations more effective

# Decongestants

- Topical
  - Oxymetazoline (Afrin)
  - Phenylephrine (neo-synephrine)
  - Instant gratification
  - Rhinitis medicamentosa with chronic use (>3-5 days)

# Decongestants

- Oral decongestants CI in patients on MAOIs
- Use caution in patients with hypertension, thyroid disease, coronary artery disease, or glaucoma

# Anticholinergics

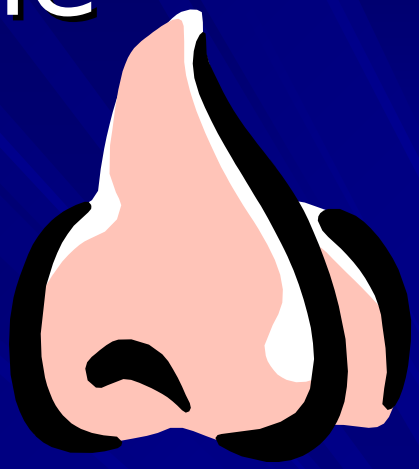
## Ipatropium bromide (Atrovent) NS

- Inhibits parasympathetic (cholinergic) nervous system
  - Decreases nasal hyperresponsiveness
  - Best for secretory/rhinorrhea symptoms
- Short acting

# Anticholinergics

- Few side effects (nasal drying, minor epistaxis)
- Indications and dosing
  - Children ages 6 and up (2 sprays bid-tid)
  - Non allergic rhinitis  0.03%
  - Rhinovirus infections 0.06%

# Nasal Antihistamine



Azelastine (Astelin)

- Intranasal antihistamine spray
  - Has anticholinergic effects
- Rapid onset (2-3 hours)
- Effective for vasomotor rhinitis
- Significantly less sedation (11%)
- Bitter taste

# Nasal Antihistamine

- 2001 study published in Annals of Allergy, Asthma, and Immunology
  - Compared Azelastine nasal spray to placebo in the treatment of perennial nonallergic rhinitis
  - Azelastine significantly reduced the TVRSS from baseline compared with placebo
  - Improvement noted within the first week
  - Bitter taste was only adverse experience

# Nasal Antihistamine

Table 3. Mean Numerical and Mean Percent Improvement in the TVRSS

| | Analysis | Treatment | N** | Mean Baseline TVRSS | Numerical Improvement in TVRSS | | | Percent Improvement in TVRSS | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Mean | SEM | *P*-value | Mean | SEM | *P*-value |
| Study No. 1 | Overall* | Azelastine | 111 | 6.51 | 1.54 | 0.14 | .002 | 24.0 | 2.11 | <.001 |
| | | Placebo | 107 | 6.54 | 0.84 | 0.17 | | 11.2 | 2.77 | |
| | Endpoint | Azelastine | 111 | 6.51 | 1.96 | 0.19 | .049 | 28.7 | 2.79 | 0.03 |
| | | Placebo | 107 | 6.54 | 1.26 | 0.21 | | 18.0 | 3.41 | |
| Study No. 2 | Overall* | Azelastine | 97 | 6.52 | 1.54 | 0.16 | .005 | 22.1 | 2.84 | .007 |
| | | Placebo | 99 | 6.65 | 0.98 | 0.16 | | 11.7 | 2.75 | |
| | Endpoint | Azelastine | 97 | 6.52 | 1.96 | 0.22 | .004 | 26.5 | 3.33 | .007 |
| | | Placebo | 99 | 6.65 | 1.01 | 0.23 | | 13.3 | 3.75 | |

TVRSS = Total Vasomotor Rhinitis Score; SEM = Standard Error of the mean

* Overall = Primary Efficacy Variable – average of all available patient data

Endpoint = each patient's last observation after baseline

** In Study No. 1, two patients in the azelastine group and three patients in the placebo group were excluded from the analysis because of no postbaseline data. In Study No. 2, six patients in the azelastine group and one patient in the placebo group were excluded from the analysis because of no postbaseline data.

# Any Questions?